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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/692,077	10/19/2000	Kersten M. Small	13105	6315

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EXAMINER
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SWITZER, JULIET CAROLINE

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 07/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/692,077

Applicant(s)

SMALL ET AL.

Examiner

Juliet C. Switzer

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 09 May 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-2, 16-17, 19-29, and 45-67 is/are pending in the application.
- 4a) Of the above claim(s) 23-29, 45-62 and 64 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 16, 17, 19-22, 63 and 65-67 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendments and arguments set forth in the response received 5/9/06 have been considered but are not sufficient to place the claims in condition for allowance. Applicant's remarks are addressed throughout the office action, as appropriate. Claims 1-2, 16-17, 19-29, and 45-67 are pending. Claims 23-29 and claims 45-62 and 64 are withdrawn from prosecution as being drawn to non-elected subject matter.

2. The change in power of attorney and statement under 37 CFR 3.73(b) filed 7/11/06 have been entered into the application.

### ***Claim Rejections - 35 USC § 112***

3. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 is indefinite because the phrase "the oligonucleotide" lacks proper antecedent basis in the claims since neither claim 22 nor any of the claims from which it depends previously recite an oligonucleotide.

*Claim Rejections - 35 USC § 112*

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 2, 16, 17, 19, 20, 21, 22, 63, 65, 66, and 67 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

In the instantly rejected claims, the new limitation of "establishing that a ligand-binding function of said alpha-2B-adrenergic receptor is reduced if said deletion polymorphism is present as compared to said ligand-binding function if said deletion polymorphism is absent" in the independent claims appears to represent new matter. The remarks suggested three possible locations for support for this limitation, but none of these provide support for the breadth of this limitation regarding decrease in any type of ligand binding function. At page 9 of the specification, lines 22-25, applicant teaches that the polymorphism showed "altered or decreased receptor coupling." This is not basis for the amendment because receptor coupling refers to a process which is the result of ligand binding where the receptor "couples" with another molecule. This is not a broad recitation that all ligand-binding function is decreased. Applicant

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further points to page 66, lines 13-18 which refers to lower phosphorylation of the deletion receptor and decrease in receptor coupling, but does not speak to the level of ligand binding. Applicant refers to Table 2 to support the amendment, but table 2 does not provide any broadly stated or exemplified demonstration of consistent decrease in ligand binding as is broadly stated in the claims. Finally applicant refers to p. 63 in its entirety, but this page refers to a small decrease in binding for a single ligand (antagonist [3H]yohimbine) but concludes in the same paragraph that the data suggest that there is little if any effect of the deletion in the conformation of the ligand binding pocket within the transmembrane spanning domains. Thus, considering as a whole the specification, applicant does not appear to have been in possession of a method as claimed, namely where one establishes that the presence of the deletion means that there is a decrease in ligand-binding function for the receptor. Since no basis has been identified, the claims are rejected as incorporating new matter.

6. Claims 1, 2, 16, 17, 19, 20, 21, 22, 63, 65, 66, and 67 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to methods for establishing an alpha-2B-adrenergic receptor function. The claims require detecting the presence or absence of a particular deletion polymorphism and set forth a step of establishing that a ligand-binding function of said receptor is reduced if the deletion polymorphism is present compared to said ligand-binding function if

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said deletion polymorphism is absent. Thus, the nature of the invention depends on the knowledge of a reliable association between the presence of the deletion allele and decreased ligand binding function.

The specification teaches a nucleic acid polymorphism within the gene encoding the  $\alpha$ -2B-adrenergic receptor molecule that results in a three amino acid deletion in the encoded polypeptide. This deletion results in the loss of three glutamic acid residues from the encoded polypeptide, these three residues being within region of the receptor that is highly acidic within the third intracellular loop (specification, Figure 2, and Jewell-Motz et al., abstract). The specification teaches the detection of the polymorphism (Example 1), the production of host cells expressing both alleles of the gene, and a series of tests of the activities of the expressed receptors. The results of these experiments are discussed beginning at page 62 of the specification. The specification teaches that "Taken together, the data suggest that there is little, if any, effect of the deletion in the third intracellular loop on the conformation of the ligand binding pocket within the transmembrane spanning domains (p. 63, lines 15-17)." The examples provided in the specification were subsequently disclosed in a journal article published by the instant inventors (with some additional authors), see Small et al., *The Journal of Biological Chemistry*, Vol. 276, No. 7, pages 4917-4922 (as cited in IDS received 3/13/03). In the abstract summarizing the same examples described in the instant specification, Small et al. wrote, regarding the effect of the polymorphism, "Ligand binding was not affected, although a small decrease in coupling efficiency to the inhibition of adenylyl cyclase was observed with the mutant." Thus, the instant specification does not appear to provide any evidence that the presence of the deletion allele is sufficient to establish that ligand-binding function is decreased

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in the deletion variant. Further, even if the data in the specification establish decreased ligand binding for a specific ligands tested, it is clearly unpredictable which additional ligands this could be applied to since the results differ for both of the tested ligands. It appears the response to one ligand might not be able to be applied to other ligands.

At the time the invention was made, there was no study of phenotypic effects the instantly disclosed polymorphism, and the current claims are limited to detecting a deletion that exclusively consists of a deletion at nucleotide positions 901 to 909 of SEQ ID NO: 1. Jewell-Mott et al. studied deletion and substitution mutants which encode an  $\alpha$ -2B-adrenergic receptor molecule with deletion or substitution of a sixteen amino acid stretch from the receptor, the deletion including the deletion of the three amino acids which are deleted as a result of the polymorphism disclosed in the instant application. Jewell-Mott et al. found that neither deletion nor substitution of the entire region did not effect ligand binding (p. 11949, 2<sup>nd</sup> column) for any tested ligand, including for the ligand [3H]yohimbine.

Thus, it is highly unpredictable whether or not the deletion polymorphism at nucleotides 901-909 of instant SEQ ID NO: 1 is sufficient to cause a reduction of ligand-binding function in the encoded  $\alpha$ -2B-adrenergic receptor molecule.

Having carefully considered all of these factors, it is concluded that at the time the invention was made, the specification was not enabling to practice the claimed invention because the specification has not provided evidence that the deletion mutation at nucleotides 901-909 of instant SEQ ID NO: 1 is sufficient to cause a reduction of ligand-binding function, and the prior art suggests that the entire region which contains this mutation is not necessary to retain ligand-binding function, and the post-filing date art summarized data identical to that in the instant

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specification as showing that this polymorphism does not effect ligand-binding in the encoded polypeptide.

**Response to Remarks; Withdrawn rejections**

Applicant's remarks are addressed in the order that they are provided.

The New Matter objection to the specification is overcome by the amendment to correct the original error. Applicant's arguments that the correction is of an obvious error are persuasive.

All previously set forth claim objections and rejections are overcome by the amendments to the claims, and so the discussion of the remainder of applicant's remarks is moot.

7. No claim is allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday, Tuesday, or Thursday, from 9:00 AM until 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached by calling (571) 272-0735.

The fax phone numbers for the organization where this application or proceeding is assigned are (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.



Juliet C. Switzer  
Primary Examiner  
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July 12, 2006